Remarks

Currently Claims 1-8, 12 and 14-20 are pending. Claims 6, and 16-17 are amended herein. Claim 6 is amended to depend from claim 1. Claims 16 and 17 are amended to recite a method for treatment of a depressive state and wherein the depressive state is a Major Depressive Disorder, respectively. New claims 19-20 are added. Support for claims 16-20 may be found through out Applicants specification, including at pages 9-12. Claims 9-11 and 13 were canceled in the prior amendment. No new matter is added. Entry of the foregoing amendments is respectfully requested.

Traversal of the Restriction Requirement

Claims 1-8, 12 and 14-18 are subject to restriction requirement.

Applicants wish to thank the Examiner for the time and courtesies extended during the telephone conferences of 12 and 14 Feb 08, during which time the outstanding restriction requirement was discussed. No agreement was reached.

The Office Action purports to divide the instant invention into multiple patent applications with claims defined where R^1 is limited to a particular ring (e.g., pyrrolidinyl in Group I, piperdyl in group II, and morpholinyl in group III). The Examiner's reasons for dividing the invention in this manner are to facilitate search because the USPTO classification index classifies these rings in different subclasses.

Applicants submit that the Examiner's restriction requirement is in clear violation of the unity of invention standard because it improperly considers the PTO classification system as a factor justifying restriction the invention, it fails to apply the standard set by the PCT for evaluating unity of a Markush group, and because it fails to identify groupings which accommodate the full scope claimed invention as defined by R^1, which can be 5-6 memebered heteroaryl or 4,5,or 6 membered heterocycle. As a result of the improper application of unity of invention and the arbitrary, capricious and incomplete assignment of subject matter in the proposed claim groupings, the office action is rendered so unclear as to preclude a complete response by Applicants. An election of one of the Examiner's groups is not possible in light of the deficiencies of the office action.

Unity of invention is met where all inventions are so linked as to form a single general inventive concept. PCT Rule13.1. More particularly, unity exists when there is a technical relationship among the claimed inventions involving one or more of the same or corresponding "special technical features." PCT Rule 13.2. Special technical features are those technical features that define a contribution which each of the inventions makes over the prior art. PCT Rule 13.2. The Examiner applies a tortured interpretation of the rule by arguing that no consideration at all should be given to the nature of any variables, numbers of variables or locations of substituents. The Office Action conveniently fails to identify what is considered under this interpretation to be the common feature for purposes of evaluating unity. Applicants can only assume that the Examiner's analysis reduces the claimed structure to merely the amide (i.e., -N-C(O)-). It appears that the purpose for this interpretation is to support the improper justification for dividing the invention in the manner sought by the Examiner –namely to apply the PTO classification index as the standard by which the claimed invention will be divided into the smallest possible units. The end result is effectively to deny Applicants their legal right to present claims which include alternatives and to deny Applicants the full scope of their invention.

The Examiner's restriction is among the members of the Markush group defining R^1. Fortunately, the MPEP provides explicit instruction and examples of how claims including Markush practice should be reviewed under the unity of invention standard. MPEP Administrative Instruction, Annex B Unity of Invention (f). The Examiner is bound by the standards and examples set forth in the MPEP. As an administrative body, the PTO has promulgated the MPEP as it's rules for practice and as such, the PTO is bound by it.

According to the MPEP, in the situation where a single claim defines alternatives,

> "the requirement of a technical interrelationship and the same or corresponding special technical feature as defined in Rule 13.2, shall be considered to be met when the alternatives are of a similar nature." MPEP AI, Annex B (f) pg AI-59.
>
> (i) When the Markush grouping is for alternatives of chemical compounds, they shall be regarded as being of similar nature where the following criteria are fulfilled:

(A) all alternatives have a common property or activity, and

(B)(1) a common structure is present, i.e., a signification structural element is shared by all of the alternatives, **or**

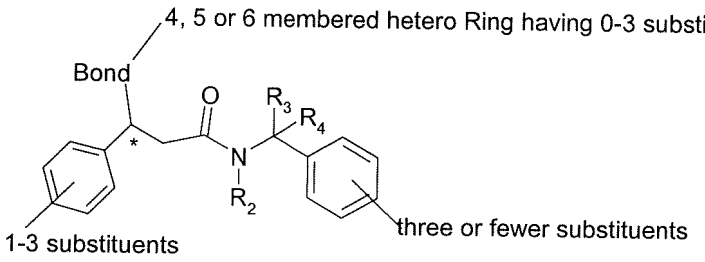
(B)(2) in cases where the common structure cannot be the unifying criteria, all alternatives belong to a recognized class of chemical compounds in the art to which the invention pertains. "

(ii) A significant structural element, pursuant to (f)(i)(B)(1), is present where the compounds share a common chemical structure which occupies a large portion of their structures, **OR** in case the compounds have in common only a small portion of the structure, the commonly shared structure is distinctive in view of the art." MPEP AI, Annex B (f)(i)-(ii) pg AI-59 (emphasis added).

A further important MPEP Rule is MPEP AI, Annex B (f)(iv): "The fact that the alternatives of a Markush grouping can be differently classified shall not, taken alone, be considered to be justification for finding a lack of unity of invention." (emphasis added)

Thus, according to the rules set out by the USPTO for examination of unity of invention in the context of Markush groups, the common structural element need not define over the prior art where the common element occupies a large portion of the structure. This is contrary to the Examiner's argument, wherein the fact that the common elements occupy a large portion of the claimed structures in the instant case was completely disregarded in favor of the method of arbitrarily disregarding certain common elements of the claimed structure in order to define the common element as a portion so small as to not define over any art.

Considering the entire claimed structure, Applicants' compounds share a common utility (as pharmaceutical agents) and common chemical elements which occupy a large portion of their structures. Accordingly unity of invention is met. In particular the common elements of the claimed structures can be represented as follows:



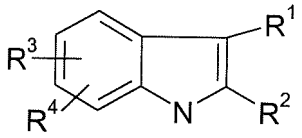
In the claimed structure, L is defined as a bond (either single or double) to a ring (R_1), the phenyl bearing (R)n being substituted with 1, 2 or 3 substituents and the phenyl bearing (R_5)m being unsubstituted or substituted 1, 2 or 3 times. All of the claimed compounds bear these common features and it is hard to imagine how the common elements could occupy a larger portion of the claimed structure. R^1 is defined as a ring of no more than 6 members. Consequently, the size of R^1 is not so large that the portion of the molecule occupied by the common elements is rendered small by comparison to the portion occupied by R_1. Because the common elements occupy a large portion of the structure, it is not necessary that those common elements differentiate over the prior art. PCT Rule 13.2; MPEP AI, Annex B (f)(i)-(ii) pg AI-59.

Given that the compounds share the same activity (as pharmaceuticals), and that they all possess a common structural element that occupies a large portion of the structures, the requirements of Rule 13.2, Annex B(f)(i) are satisfied and unity of invention is met.

As suggested in MPEP AI, Annex B(I), the Examiner is respectfully requested to consult the numerous examples provided in the PCT International Searching and Preliminary Examination Guidelines for examining unity in a Markush group.

"10.38 *Example 18: common structure:*

"Claim 1: A compound of the formula:



wherein R_1 is selected from the group consisting of phenyl, pyridyl, thiazolyl, triazinyl, alkylthio, alkoxy, and methyl; R_2-R_4 are methyl, benzyl, or phenyl. The compounds are useful as pharmaceuticals for the purpose of enhancing the capacity of the blood to absorb oxygen.

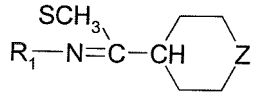
> In this case the indolyl moiety is the significant structural element that is shared by all of the alternatives. Since all the claimed compounds are alleged to possess the same utility, **unity is present**." PCT/GL/ISPE/1 10.38, Example 18, pg 84 (emphasis added).

The Examiner should note that the indolyl moiety in this example clearly cannot be said to define over the prior art. It does however provide a common element that occupies a large portion of the chemical structure of all compounds claimed. As such, it is not necessary that the indolyl define over the prior art. Further, the definition of the variable R^1 in the foregoing MPEP example includes a 6-membered aromatic ring having no heteroatoms, two different 6-membered heteroaryl rings, and a 5-membered heteroaryl ring, all in the same Markush group, and yet unity is present. This example is directly on point with the instant case. There is no basis for the Examiner's attempt to segregate between the specific rings. Note that the foregoing example does not indicate that unity is lacking and that the inventions must be divided into separate groups wherein 1) R^1 is phenyl, 2) R^1 is pyridyl, 3) R^1 is thiazolyl, etc. Nor is there any basis in the foregoing example for the Examiner to divide the claimed invention based on the size of the ring. Based on this example, when the common elements occupy a large portion of the claimed structure, there is no grounds for a lack of unity rejection.

According to the PCT Guidelines, unity of invention is also met in the following example:

10.39 *Example 19: common structure:*

Claim 1: A compound of the formula:



wherein R1 is selected from the group consisting of phenyl, pyridyl, thiazolyl, triazinyl, alkylthio, alkoxy, and methyl; Z is selected from the group consisting of oxygen (O), sulfur (S), imino (NH), and methylene (-CH2-).
The compounds are alleged to be useful as pharmaceuticals for relieving lower back pain.

> In this particular case the iminothioether group -N=C-SCH3 linked to a six atom ring is the significant structural element which is shared by all the alternatives. Thus, since all the claimed compounds are alleged to possess the same use, unity would be present." PCT/GL/ISPE/1 10.38, Example 18, pg 84 (emphasis added).

This MPEP Example demonstrates that the Examiner is not permitted to disregard variables when determining the common elements of the structure. Note that the guidelines define the common structure as including a six-membered ring. Under the Examiner's analysis, the variable Z would have been disregarded and the common elements of the structure would have been reduced to the group (—N=C(SCH_3)—). Had no consideration been given to how Z is defined, the exemplar could not have concluded that the iminothioether group was bound to a six-membered ring. If Z had been defined in this example as a bond, the result would not have been a six-membered ring. The Examiner must consider the definition of Z in order to conclude that the common structure includes a 6 membered ring. In addition, this example further emphasizes the teaching above regarding Markush group analysis. The Examiner should note the definition of the variable R_1, which includes a 6-membered aromatic ring having no heteroatoms, two different 6-membered heteroaryl rings, and a 5-membered heteroaryl ring, and yet unity is present as was the case in the previous example. Twice then, the MPEP's Administrative Instructions for Examining unity of invention in a Markush group directly conflict with the position taken by the Examiner in this case.

The Examiner is encouraged to review the PCT Guidelines for further examples, but the foregoing clearly demonstrate that unity of invention is present in the instant case and there is no basis for requiring any restriction among the claims, including the process and method claims. See MPEP AI, Annex B(e)(i).

Applicants understand the limited time available to the Examiner for searching and the Examiner's resulting desire to narrow the field of search. Yet, the Examiner's argument that the search is burdensome due to the reliance on the PTO classification manual is a red herring. Prior to the introduction of methods for electronically searching chemical structures, the PTO classification index played a predominant role in searching chemical structures. The flagrant inefficiencies of that system are now readily apparent in light of the newer technology currently employed by the office. The search conducted by the Examiner will be foremost an electronic search based on chemical structure. The assertion that the search will be manually conducted using only the PTO classification index is directly contrary to the clear weight of evidence in PAIR, where in every chemical case, an Examiner's electronic search strategy is made of record.

What will become burdensome, for both the Office and Applicants is to divide Applicants' invention in the manner suggested by the Examiner. A separate divisional application claiming a single specific ring for R_1 will result in hundreds of divisional applications. Each separate divisional for a particular compound would have a corresponding divisional for a process claim for making the same, and further one or more separate divisional applications for each method of using the same. This Examiner will be inundated with these divisional applications. Ironically, if Applicants had initially chosen to file all of those applications separately the Examiner would be faced with the daunting task of analyzing obviousness-type double patenting for those same hundreds of cases. This would paralyze the office into a far greater backlog than it already alleges exists. This outcome serves neither Applicants' interest, nor the interests of the PTO in efficient examination.

As explained during the telephone conferences of 12 and 14 Feb 2008, Applicants wish to work with the Examiner to reach a compromise that will facilitate the thorough, yet timely examination of this claimed invention. Accordingly, Applicants respectfully request that the Examiner reconsider Applicants proposed alternative restriction, which follows:

Group I: claims 1-7, 12, 14 and 15, drawn to compounds and compositions of formula I, wherein R_1 is a 5 or 6 membered heteroaryl;

Group II: claims 1-7, 12, 14 and 15, drawn to compounds and compositions of formula I, wherein R_1 is a 4, 5 or 6 membered heterocycle;

Group III: claim 8 drawn to a process for preparing compounds of Group I;

Group IV: claim 8 drawn to a process for preparing compounds of Group II;

Group V: claims 16-18 drawn to a method of treating a depressive state with a compound of Group I;

Group VI: claims 16-18 drawn to a method of treating a depressive state with a compound of Group II;

Group VII: new claim 19 drawn to a method of treating anxiety with a compound of Group I;

Group VIII: new claim 19 drawn to a method of treating anxiety with a compound of Group II;

Group IX; new claim 20 drawn to a method of treating rheumatoid arthritis with a compound of Group I; and

Group X: new claim 20 drawn to a method of treating rheumatoid arthritis with a compound of Group II.

Should the Examiner, upon reconsideration, agree with this suggested restriction, Applicants elect without traverse, the claims of Applicants' Group II, claims 1-7, 12, 14 and 15, drawn to compounds and compositions of formula (I), wherein R_1 is a 4, 5 or 6 membered heterocycle. Applicants further elect the single species of Example 1. The election of species is made with the understanding that upon the finding of an allowable species, examination will continue with the non-elected species until all species have been examined or a non-allowable species is found.

Further, upon receipt of the Examiner's affirmation of this restriction, Applicants will extend the courtesy of giving consideration to whether any rejoinder of the foregoing groups will be sought versus immediately filing 9 new divisional patent applications, in order to facilitate the efficient examination of the full scope of the claimed invention.

The Examiner rejected Applicants proposed restriction during the telephone conference of 14 Feb 2008, and instead suggested a modified restriction resulting in separate applications for embodiments wherein R_1 is a 5 membered heteroaryl, R_1 is a 6 membered heteroaryl, R_1 is a 4 membered heterocycle, R_1 is a 5 membered heterocycle, and R_1 is a 6 membered heterocycle. Applicants understand the Examiner's new proposed restriction to result in the following groupings for the pending claims:

Group 1: claims 1-7, 12, 14 and 15, drawn to compounds and compositions of formula I, wherein R_1 is a 5 membered heteroaryl;
Group 2: claims 1-7, 12, 14 and 15, drawn to compounds and compositions of formula I, wherein R_1 is a 6 membered heteroaryl;
Group 3: claims 1-7, 12, 14 and 15, drawn to compounds and compositions of formula I, wherein R_1 is a 4 membered heterocycle;
Group 4: claims 1-7, 12, 14 and 15, drawn to compounds and compositions of formula I, wherein R_1 is a 5 membered heterocycle;
Group 5: claims 1-7, 12, 14 and 15, drawn to compounds and compositions of formula I, wherein R_1 is a 6 membered heterocycle;

Group 6: claim 8 drawn to a process for preparing compounds of Group 1;

Group 7: claim 8 drawn to a process for preparing compounds of Group 2;

Group 8: claim 8 drawn to a process for preparing compounds of Group 3;

Group 9: claim 8 drawn to a process for preparing compounds of Group 4;

Group 10: claim 8 drawn to a process for preparing compounds of Group 5;

Group 11: claims 16-18 drawn to a method of treating a depressive state with a compound of Group 1;

Group 12: claims 16-18 drawn to a method of treating a depressive state with a compound of Group 2;

Group 13: claims 16-18 drawn to a method of treating a depressive state with a compound of Group 3;

Group 14: claims 16-18 drawn to a method of treating a depressive state with a compound of Group 4;

Group 15: claims 16-18 drawn to a method of treating a depressive state with a compound of Group 5;

Group 16: new claim 19 drawn to a method of treating anxiety with a compound of Group 1;

Group 17: new claim 19 drawn to a method of treating anxiety with a compound of Group 2;

Group 18: new claim 19 drawn to a method of treating anxiety with a compound of Group 3;

Group 19: new claim 19 drawn to a method of treating anxiety with a compound of Group 4;

Group 20: new claim 19 drawn to a method of treating anxiety with a compound of Group 5;

Group 21; new claim 20 drawn to a method of treating rheumatoid arthritis with a compound of Group 1;

Group 22: new claim 20 drawn to a method of treating rheumatoid arthritis with a compound of Group 2;

Group 23: new claim 20 drawn to a method of treating rheumatoid arthritis with a compound of Group 3;

Group 24: new claim 20 drawn to a method of treating rheumatoid arthritis with a compound of Group 4;

Group 25: new claim 20 drawn to a method of treating rheumatoid arthritis with a compound of Group 5;

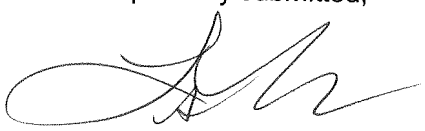
In the event that the Examiner maintains this restriction, Applicants elect with traversal (for the reasons set forth above) the Examiners newly proposed Group 5, claims 1-7, 12, 14 and 15, drawn to compounds and compositions of formula I, wherein R_1 is a 6 membered heterocycle. The traversal is on the grounds that the unity of invention standard was not properly applied and as such, the Examiner is not entitled to conclude that each claim grouping is obvious over the other.

The foregoing election of species is applicable, on the same provision regarding further examination.

If this election is maintained, no traversal on the grounds that the groups are obvious over the other and no request for rejoinder will be made. Rather Applicants may promptly exercise their right to file separate divisional applications directed toward each of the Examiner's 25 defined groups.

Substantive examination of the instant application is respectfully requested. The Examiner is invited to contact the undersigned at (919) 483-8222, to discuss this case or the restriction requirement further, if desired.

Respectfully submitted,



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